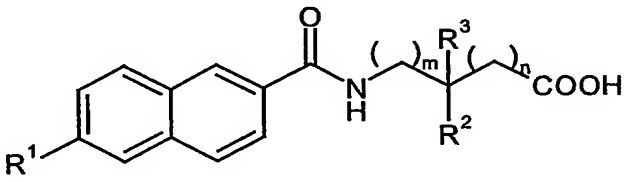
Claims

(1) A 2-naphthamide derivative of the formula (I), its tautomeric or stereoisomeric form, or a salt thereof:



(I)

wherein

m and n independently represent an integer from 0 to 2;

$-R^1$ represents $-O-R^{10}-OR^{11}$, $-OR^{11}$, $-SR^{11}$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-NR^{12}R^{13}$, or $-CHR^{14}R^{15}$,

wherein

$-R^{10}-$ represents (C_{1-6}) alkylene;

R^{11} represents aryl, (C_{2-6})alkenyl optionally substituted by aryl or heteroaryl, (C_{2-6})alkynyl optionally substituted by aryl or heteroaryl, or (C_{1-6}) alkyl optionally substituted by (C_{3-8})-cycloalkyl, aryl or heterocycle comprising 4-9 carbons and at least one N, O, or S as a heteroatom,

wherein

said (C_{3-8})cycloalkyl, aryl and heterocycle optionally have one or two substituents selected from the group consisting of halogen, hydroxy, nitro, (C_{1-6}) alkyl optionally substituted by

mono-, di-, or tri halogen, and (C_{1-6}) alkoxy optionally substituted by (C_{3-8})cycloalkyl, or mono-, di-, or tri halogen;

R^{12} and R^{13} independently represent hydrogen, (C_{2-6})alkenyl optionally substituted by aryl or heteroaryl, (C_{2-6})alkynyl optionally substituted by aryl or heteroaryl, or (C_{1-6}) alkyl optionally substituted by aryl or heteroaryl,

or

R^{12} and R^{13} form, together with the nitrogen atom, a 5-7 membered saturated hetero ring optionally interrupted by O or NH;

R^{14} and R^{15} independently represent hydrogen, (C_{2-6})alkenyl optionally substituted by aryl or heteroaryl, (C_{2-6})alkynyl optionally substituted by aryl or heteroaryl, (C_{1-6}) alkyl optionally substituted by aryl or heteroaryl, or (C_{1-6}) alkoxy optionally substituted by aryl or heteroaryl,

or

R^{14} and R^{15} form, together with the CH, a (C_{3-8})cycloalkyl optionally interrupted by NH, or O, or a phenyl optionally substituted by hydroxy, halogen or (C_{1-6}) alkyl;

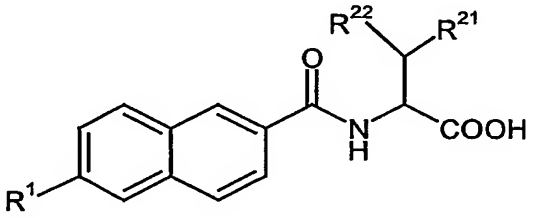
R^2 represents hydrogen, hydroxy, cyano, (C_{1-6}) alkoxy, (C_{2-6})alkenyl, (C_{2-6})alkynyl, (C_{3-7})cycloalkyl, or (C_{1-6}) alkyl optionally having one or two substituents selected from the group consisting of hydroxy, amino, (C_{1-6})alkylamino, aryl, and heteroaryl comprising 4-10 carbons and at least one N, O, or S as a heteroatom,

wherein

said aryl and heteroaryl optionally have one or two substituents selected from the group consisting of halogen, hydroxy, nitro, amino, N((C_{1-6}) alkyl sulfonyl)amino, morpholino, phenyl, pyridyl, (C_{1-6}) alkoxy optionally substituted by mono-, di-, or tri halogen, and (C_{1-6}) alkyl optionally substituted by mono-, di-, or tri halogen; and

R^3 represents hydrogen, or (C_{1-6}) alkyl.

(2) A 2-naphthamide derivative of the formula (I'), its tautomeric or stereoisomeric form, or a salt thereof:



(I')

wherein

$-R^1$ represents $-O-R^{10}-OR^{11}$, $-OR^{11}$, $-SR^{11}$, $-S(O)R^{11}$, $-S(O)_2R^{11}$, $-NR^{12}R^{13}$, or $-CHR^{14}R^{15}$,

wherein

$-R^{10}-$ represents (C_{1-6}) alkylene;

R^{11} represents aryl, (C_{2-6})alkenyl optionally substituted by aryl or heteroaryl, (C_{2-6})alkynyl optionally substituted by aryl or heteroaryl, or (C_{1-6}) alkyl optionally substituted by (C_{3-8})-

cycloalkyl, aryl or heterocycle comprising 4-9 carbons and at least one N, O, or S as a heteroatom

wherein

said (C_{3-8})cycloalkyl, aryl and heterocycle optionally have one or two substituents selected from the group consisting of halogen, hydroxy, nitro, (C_{1-6}) alkyl optionally substituted by mono-, di-, or tri halogen, and (C_{1-6}) alkoxy optionally substituted by (C_{3-8})cycloalkyl, or mono-, di-, or tri halogen;

R^{12} and R^{13} independently represent hydrogen, (C_{2-6})alkenyl optionally substituted by aryl or heteroaryl, (C_{2-6})alkynyl optionally substituted by aryl or heteroaryl, or (C_{1-6}) alkyl optionally substituted by aryl or heteroaryl,

or

R^{12} and R^{13} form, together with the nitrogen atom, a 5-7 membered saturated hetero ring optionally interrupted by O or NH;

R^{14} and R^{15} independently represent hydrogen, (C_{2-6})alkenyl optionally substituted by aryl or heteroaryl, (C_{2-6})alkynyl optionally substituted by aryl or heteroaryl, (C_{1-6}) alkyl optionally substituted by aryl or heteroaryl, or (C_{1-6}) alkoxy optionally substituted by aryl or heteroaryl,

or

R^{14} and R^{15} form, together with the CH, a (C_{3-8})cycloalkyl optionally interrupted by NH, or O, or a phenyl optionally substituted by hydroxy, halogen or (C_{1-6}) alkyl;

R^{21} represents hydroxy, cyano, amino, (C_{1-6})alkylamino, thienyl, pyridyl, phenyl, naphthyl, 1H-pyrrolo[2,3-b]pyridin-3-yl, or indolyl optionally substituted by halogen or hydroxy,

wherein

said phenyl and naphthyl optionally have one or two substituents selected from the group consisting of halogen, hydroxy, nitro, amino, N((C_{1-6}) alkyl)amino, di(C_{1-6}) alkylamino, N((C_{1-6}) alkyl sulfonyl)-amino, morpholino, phenyl, pyridyl, (C_{1-6}) alkoxy optionally substituted by mono-, di-, or tri halogen, and (C_{1-6}) alkyl optionally substituted by mono-, di-, or tri halogen; and

R^{22} represents hydrogen or hydroxy.

(3) The 2-naphthamide derivative, its tautomeric or stereoisomeric form, or a salt thereof as claimed in claim 1 or 2,

wherein

R^1 represents phenoxy, (C_{1-6}) alkoxy optionally substituted by cyclopropyl, cyclohexyl, pyrrolidinyl, piperidinyl, imidazolyl, pyridyl, pyrrolyl, thiazolyl optionally substituted by (C_{1-6})alkyl, or phenyl,

wherein

said phenyl optionally has one or two substituents selected from the group consisting of fluoro, chloro, bromo, nitro, hydroxy, (C_{1-6})alkyl optionally substituted by mono-, di, or tri halogen, and (C_{1-6}) alkoxy optionally substituted by mono-, di, or tri halogen, cyclopropyl, or cyclohexyl.

(4) The 2-naphthamide derivative, its tautomeric or stereoisomeric form, or a salt thereof as claimed in claim 1 or 2,

wherein

R^1 represents phenoxy(C_{1-6})alkyl, phenoxy(C_{1-6})alkenyl, phenoxy(C_{1-6})-alkynyl, or phenyl(C_{1-6})alkoxy.

(5) The 2-naphthamide derivative, its tautomeric or stereoisomeric form, or a salt thereof as claimed in claim 1,

wherein

R^2 represents phenyl (C_{1-6})alkyl,

wherein

said phenyl optionally has one or two substituents selected from the group consisting of fluoro, chloro, bromo, iodo, hydroxy, nitro, amino, N(methanesulfonyl)amino, morpholino, phenyl, pyridyl, methoxy, ethoxy, and trifluoromethyl.

(6) The 2-naphthamide derivative, its tautomeric or stereoisomeric form, or a salt thereof as claimed in claim 2,

wherein

R^1 represents phenoxy, (C_{1-6}) alkoxy optionally substituted by cyclopropyl, cyclohexyl, pyrrolidinyl, piperidinyl, imidazolyl, pyridyl, pyrrolyl, phenyl, or thiazolyl optionally substituted by (C_{1-6})alkyl,

wherein

said phenyl has optionally one or two substituents selected from the group consisting of fluoro, chloro, bromo, nitro, hydroxy, (C_{1-6})alkyl optionally substituted by mono-, di, or tri halogen, and (C_{1-6}) alkoxy optionally substituted by mono-, di, or tri halogen, cyclopropyl, or cyclohexyl;

R^{21} represents cyano, thienyl, pyridyl, phenyl, naphthyl, 1H-pyrrolo[2,3-b]pyridin-3-yl, or indolyl optionally substituted by halogen or hydroxy,

wherein

said phenyl and naphthyl have one or two substituents selected from the group consisting of fluoro, chloro, bromo, hydroxy, nitro, amino, N((C_{1-6}) alkyl)amino, di(C_{1-6}) alkylamino, N((C_{1-6}) alkyl sulfonyl)-amino, morpholino, phenyl, pyridyl, trifluoromethyl, trifluoromethyloxy, (C_{1-6}) alkoxy, and (C_{1-6}) alkyl; and

R^{22} represents hydrogen or hydroxy.

(7) The 2-naphthamide derivative, its tautomeric or stereoisomeric form, or a salt thereof as claimed in claim 1 or 2,

wherein

R^{12} and R^{13} independently represent hydrogen, or (C_{1-6}) alkyl optionally substituted by phenyl, naphthyl or pyridyl.

(8) The 2-naphthamide derivative, its tautomeric or stereoisomeric form, or a salt thereof as claimed in claim 1, wherein said derivative is selected from the group consisting of the following compounds:

N-[6-(benzyloxy)-2-naphthoyl]phenylalanine;
N-[6-(benzyloxy)-2-naphthoyl]-4-(trifluoromethyl)phenylalanine;
N-{6-[(4-fluorobenzyl)oxy]-2-naphthoyl}phenylalanine;
N-{6-[(3-fluorobenzyl)oxy]-2-naphthoyl}phenylalanine;
N-{6-[(2-fluorobenzyl)oxy]-2-naphthoyl}phenylalanine;
N-[6-(3-pyridinylmethoxy)-2-naphthoyl]phenylalanine;
N-{6-[(3,4-difluorobenzyl)oxy]-2-naphthoyl}phenylalanine;
N-{6-[2-(1H-pyrrol-1-yl)ethoxy]-2-naphthoyl}phenylalanine;
N-[6-(4-pyridinylmethoxy)-2-naphthoyl]phenylalanine;
N-[6-(benzyloxy)-2-naphthoyl]-3-(trifluoromethyl)phenylalanine;
N-[6-(benzyloxy)-2-naphthoyl]tryptophan;
N-[6-(benzyloxy)-2-naphthoyl]-O-methyltyrosine;
N-[6-(benzyloxy)-2-naphthoyl]-3-methoxytyrosine;
N-[6-(benzyloxy)-2-naphthoyl]-β-hydroxyphenylalanine;
N-[6-(2-phenylethoxy)-2-naphthoyl]phenylalanine;
N-[6-(benzyloxy)-2-naphthoyl]-4-chlorophenylalanine;
N-[6-(benzyloxy)-2-naphthoyl]-3-fluorophenylalanine;
N-{6-[(2-chlorobenzyl)oxy]-2-naphthoyl}phenylalanine;
N-{6-[(3-chlorobenzyl)oxy]-2-naphthoyl}phenylalanine;
N-{6-[(2-methoxybenzyl)oxy]-2-naphthoyl}phenylalanine;
N-{6-[(3-methoxybenzyl)oxy]-2-naphthoyl}phenylalanine;
N-{6-[(2,3-dichlorobenzyl)oxy]-2-naphthoyl}phenylalanine;

N-{6-[(3,5-dichlorobenzyl)oxy]-2-naphthoyl}phenylalanine;
N-{6-[(3,5-dimethoxybenzyl)oxy]-2-naphthoyl}phenylalanine;
N-[6-(benzyloxy)-2-naphthoyl]-3-(2-thienyl)alanine;
N-[6-(benzyloxy)-2-naphthoyl]-4-bromophenylalanine;
N-[6-(benzyloxy)-2-naphthoyl]-4-nitrophenylalanine;
N-[6-(benzyloxy)-2-naphthoyl]-3-hydroxyphenylalanine;
N-[6-(benzyloxy)-2-naphthoyl]-3-(1-naphthyl)alanine;
N-[6-(benzyloxy)-2-naphthoyl]-5-hydroxytryptophan;
N-[6-(benzyloxy)-2-naphthoyl]-2-fluorophenylalanine;
N-{6-[(2-bromobenzyl)oxy]-2-naphthoyl}phenylalanine;
N-{6-[(3-bromobenzyl)oxy]-2-naphthoyl}phenylalanine;
N-{6-[(2-methylbenzyl)oxy]-2-naphthoyl}phenylalanine;
N-{6-[(3-methylbenzyl)oxy]-2-naphthoyl}phenylalanine;
N-{6-[(3-nitrobenzyl)oxy]-2-naphthoyl}phenylalanine;
N-[6-(benzyloxy)-2-naphthoyl]-3-(2-naphthyl)alanine;
N-[6-(benzyloxy)-2-naphthoyl]-4-iodophenylalanine;
N-[6-(benzyloxy)-2-naphthoyl]-5-fluorotryptophan;
N-[6-(benzyloxy)-2-naphthoyl]-3-(1H-pyrrolo[2,3-b]pyridin-3-yl)alanine;
N-{6-[2-(4-pyridinyl)ethoxy]-2-naphthoyl}phenylalanine;
N-{6-[(3-ethoxybenzyl)oxy]-2-naphthoyl}phenylalanine; and
N-[6-(2-phenylpropoxy)-2-naphthoyl]phenylalanine;

(9) A medicament comprising the 2-naphthamide derivative, its tautomeric or stereoisomeric form, or a physiologically acceptable salt thereof as claimed in claim 1 as an active ingredient.

(10) The medicament as claimed in claim 9, further comprising one or more pharmaceutically acceptable excipients.

(11) The medicament as claimed in claim 9, wherein the 2-naphthamide derivative, its tautomeric or stereoisomeric form, or a physiologically acceptable salt thereof is an IP receptor antagonist.

(12) The medicament as claimed in claim 9 for prophylaxis and/or treatment of urological disorder or disease.

(13) The medicament as claimed in claim 9 for prophylaxis and/or treatment of pain.

(14) The medicament as claimed in claim 9 for prophylaxis and/or treatment of hypotension.

(15) The medicament as claimed in claim 9 for prophylaxis and/or treatment of hemophilia and hemorrhage.

(16) The medicament as claimed in claim 9 for prophylaxis and/or treatment of inflammation.

(17) Use of compounds according to claim 1 for manufacturing a medicament for the treatment and/or prophylaxis of urological disorders.

(18) Use of compounds according to claim 1 for manufacturing a medicament for the treatment and/or prophylaxis of pain.

(19) Use of compounds according to claim 1 for manufacturing a medicament for the treatment and/or prophylaxis of hypotension.

(20) Use of compounds according to claim 1 for manufacturing a medicament for the treatment and/or prophylaxis of hemophilia and hemorrhage.

(21) Use of compounds according to claim 1 for manufacturing a medicament for the treatment and/or prophylaxis of inflammation.

(22) Process for controlling urological disorders in humans and animals by administration of an IP receptor-antagonisticly effective amount of at least one compound according to claim 1.

(23) Process for controlling pain in humans and animals by administration of an IP receptor-antagonisticly effective amount of at least one compound according to claim 1.

(24) Process for controlling hypotension in humans and animals by administration of an IP receptor-antagonisticly effective amount of at least one compound according to claim 1.

(25) Process for controlling hemophilia and hemorrhage in humans and animals by administration of an IP receptor-antagonisticly effective amount of at least one compound according to claim 1.

(26) Process for controlling inflammation in humans and animals by administration of an IP receptor-antagonisticly effective amount of at least one compound according to claim 1.